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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/152,698	09/02/1998	REGUPATHY MADIYALAKAN	AREX-P02-004	4505

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 08/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/152,698	MADIYALAKAN ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) 30,71,76,85-88,96,98-100,103-114,117,119 and 123-128 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 30,71,76,85-87,96,98-100,103-114,117,119 and 123-128 is/are rejected.

7)☐ Claim(s) 88 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 10/29/04; 3/13/06.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 75, 89, 93, 95, 101, 102, 115, 116 and 120-122 have been canceled. Claims 30, 85, 103-105, 107-109 and 117-119 have been amended. Claims 123-128 have been added. Claims 30, 71, 76, 85-88, 96 and 98-100, 103-114, 117, 119 and 123-128 are pending and under consideration.

2. Text of Title 35, U.S. Code, not found in this action can be found in a previous action.

3. Claims 30, 71, 76, 85-87, 96, 98-100, 103-114, 117-119 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating an oncological disease comprising administering to a host a complex formed from CA125 and a monoclonal antibody or antigen-binding fragment thereof that binds to CA125, and wherein the complex induces host antibodies and cytotoxic T-cells reactive with at least one other epitope of the tumor associated antigen, does not reasonably provide enablement for the administration of any other complex of a soluble tumor antigen and a monoclonal antibody or antigen-binding fragment thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The prior office action rejection concluded with:

Due to the unreliability of the art as discussed above, the lack of a working example which demonstrates the successful treatment of a subject with an antigen antibody complex beyond that of Mab 43.13 bound to soluble CA125, one of skill in the art would be subject to undue experimentation without reasonable expectation of success in order to practice the broadly claimed method.

Applicant has amended the claims to be restricted to the CA125 antigen, however, the antibody which binds to said antigen is not restricted. The specification specifically demonstrates the success of the claimed method only with Mab 43.13. The specification does not provide any guidance for the selection of a different antibody which binds to CA125, nor of antibodies which bind to epitopes of CA125 that differ from the epitope bound by Mab 43.13. Thus, while other antibodies that bind the same epitope of Mab 43.13 would be expected to

function within the same method, there is no assurance from the instant specification regarding the criteria for selecting other antibodies which bind to differing epitopes of CA125 which would evoke host cytotoxic T-cells and antibodies recognize alternate epitopes of CA125. It is noted that the instant specification claims priority to WO 97/42973, filed May 15, 1996 and should be enabled as of the effective filing date sought. Madiyalakan et al (WO9965517, page 12, lines 12-30) teach:

Stimulation of T cells reactive with subdominant or cryptic epitopes of self proteins has been suggested as an important factor in inducing immunity to a predetermined antigen, e. g., an antigen involved in a disease or condition such as cancer or auto-immunity. Antibody-enhanced or-altered presentation of an antigen, such as CA125, in an antibody complex, e. g., bound to MAb-B43.13, by B cells (antibody specific), or macrophages or dendritic cells (both receptor mediated), may result in presentation of different peptides to the immune system than those obtained by presentation of the antigen alone. This can lead to sufficient presence of antigen-specific peptides from subdominant or cryptic epitopes which may in turn stimulate low affinity T cells that escaped clonal deletion in the thymus or re-stimulate T cells which were suppressed. The immune response induced by exogenous administration of an antibody to a circulating self-antigen can therefore be compared to that observed in auto-immune diseases. This may also explain why presence of immune complexes of antigen with autologous human antibodies is often not correlated with improved survival. Human B cells recognize preferably immune-dominant epitopes of the antigen, leading to presentation of epitopes against which T cells were formed during fetal development. Murine antibodies on the other hand, recognize immune-dominant epitopes in mice which are not necessarily equivalent to the human immune-dominant epitopes.

Thus, the teachings of the post-filing date art indicate that it is necessary to target subdominant epitopes of the CA125 antigen and that epitopes targeted by murine antibodies are "not necessarily equivalent" to the human dominant epitopes. Thus, the post filing reference teaches the importance of targeting an epitope which is not a dominant epitope in order to elicit antibodies and immune recognition against subdominant epitopes and that not all murine antibodies will possess the criteria of targeting an epitope which is not a dominant human

epitope. without this information published in 1997, it would be undue experimentation in order to screen all possible antibodies, including antibodies from a multitude of experimental hosts and human antibodies, for the ability to evoke antibodies to a different epitope on CA125 than that bound by the antibody or T-cell recognition of CA125.

4. Claims 30, 71, 76, 98, 99, 103-110, 113, 114, 117-119 and 123-128 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 30, 71, 76, 98, 99, 103-110, 113, 114, 117-119 and 123-128 of U.S. Patent No. 6,241,985. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of the claims of the '985 patent encompasses the instant claims. Claim 1 of the patent is drawn to "contacting" the CA125 antigen with the monoclonal antibody B43.13 and allowing the formation of a binding pair. the claim does not specify that the B43.13 antibody be administered directly to the host. The specification of '985 provides a preferred embodiment wherein a patients blood is removed and reacted with the B43.13 ex vivo and said modified blood re-administered to said patient (column 12, lines 56-62) which is within the scope of the claims for the patent and anticipated the instant claims requiring administration of the antigen-antibody complex. The claims of the '985 patent require a cellular immune response, but the cytotoxic T cells generated by the method of the instant claims would inherently generate cytotoxic T cells because the interaction between B43.13 and the CA125 antigen produces a complex which elicits a host immune response against another epitope and inherently results in the generation of cytotoxic T-cells in the method of the patent. The claims of the patent do not specify that the antibody is a IgG type antibody, however, the B43.13 antibody is an IgG type antibody as evidenced by Madiyalakan et al (WO 99/65517).

5. Claims 30, 71, 76, 98, 99, 103-110, 113, 114, 117-119 and 123-128 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 276-282, 293-302, 313-322 and 333-338 of copending Application No. 09/376,604. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '604 anticipate the instant claims to the extent that they read on the CA125 antigen.

Independent claim 276 of the '604 application is drawn to "contacting" the CA125 antigen with an antibody that binds to a first epitope wherein an effective host T-cell response is elicited to CA125; independent claim 277 is drawn to "contacting" the CA125 antigen with an antibody that binds to an epitope and host immune response against a second epitope; independent claim 278 is drawn to "contacting" the CA125 antigen with an antibody that binds to a first epitope wherein an effective host T-cell response is elicited to CA125 and effective humoral immune response is generated to a second epitope. Claims 276-278 require the formation of an immune complex, but do not specify that the immune complex is necessarily formed in vivo tot eh exclusion of ex vivo immune complex formation. The specification of '604 provides a preferred embodiment wherein a patients blood is removed and reacted with the binding agent ex vivo and said modified blood re-administered to said patient (page 41, lines 26-30) which is within the scope of the claims for the patent and anticipated the instant claims requiring administration of the antigen-antibody complex. The claims of the '604 application do not specify that the antibody is a IgG type antibody, however, claim 302 and 322 of '604 specify the B43.13 antibody, which is a IgG antibody as evidenced by Madilayakan et al (WO 99/65517).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

6. Claim 88 is maintained as objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

7. All other rejections and objections as set forth or maintained in the prior Office action are withdrawn in light of applicant's amendments.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Karen A. Canella, Ph.D.
7/24/2006

KAREN A. CANELLA PH.D
PRIMARY EXAMINER